REMARKS/ARGUMENTS

Upon entry of this Amendment, claims 1, 6-12 and 15-18 are pending and are presented for examination. Claims 2-5 have been withdrawn as being directed to a non-elected invention pursuant to a Restriction Requirement. New claims 18 and 19 have been added. In order to expedite prosecution, claim 12 has been amended and claims 13 and 14 have been cancelled without prejudice to further prosecution. Support for the amendments to claim 12 can be found, for example, on pages 17 and page 19, *i.e.*, paragraphs 69 and 87, of the specification, and in the claims as originally filed. Moreover, in order to expedite prosecution, claim 17 has been amended. Support for the amendment to claim 17 can be found, for example, on pages 11, 12, 13 and 14, *i.e.*, paragraphs 52, 54, 56 and 58, of the specification. Support for new claim 18 is found on page 21-22, Reference 3. Support for new claim 19 can be found, for example, on pages 17 and page 19, *i.e.*, paragraphs 69 and 87, of the specification. No new matter has been added by the amendments to the claims or the addition of new claims 18 and 19. Accordingly, reconsideration is respectfully requested.

I. Rejections under 35 U.S.C. §112

A. Indefinite Rejection

Claims 1 and 6-17 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention.

In order to expedite prosecution, Applicants have amended claims 1 and 17. In view of the amendments to claims 1 and 17, the Examiner's concern is overcome. Accordingly, Applicants urge the Examiner to withdraw this rejection under 35 U.S.C. §112, second paragraph.

B. Enablement Rejection

1. Prodrugs

Claims 1 and 6-17 were rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabled by the specification for making prodrugs of the claimed compounds.

In order to expedite prosecution, Applicants have amended claims 1 and 17. In view of the amendments to claims 1 and 17, the Examiner's concern is overcome. Accordingly, Applicants urge the Examiner to withdraw this rejection under 35 U.S.C. §112, first paragraph.

2. Solvate or Hydrate

Claims 1 and 6-17 were rejected as allegedly non-enabled by the specification for making solvates or hydrates of the claimed compounds. In support of this rejection, the Examiner alleges that the formation of solvates or hydrates and composition of solvates or hydrates are unpredictable. Therefore, in the absence of working examples, the Examiner alleges that undue experimentation would be required to make Applicants' invention. Applicants respectfully disagree.

The test for the enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (*see*, MPEP §2164.01). The court has stated eight unlimited factors to assess whether an experimentation is undue. Applicants assert that, if anything, only routine experimentation is needed to form solvates or hydrates of the presently claimed compounds.

The nature of the invention and the state of prior art. The Examiner alleges that the state of art is such that it is not predictable whether solvates or hydrates of a compound will form or what the composition will be (*see*, page 14 of the Office Action, citing page 358 of Anthony R. West, *Solid State Chemistry and Its Applications*, Wiley, hereinafter "West"). In traversal of the rejection, Applicants submit that West is ***not*** analogous art.

To rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or if not, then be reasonably pertinent to the particular problem with which the inventor was concerned (*see*, MPEP §2141.01(a)). A perusal of the West reference reveals that West is directed to inorganic salts and the hydrates or

solvates of such inorganic salts. West teaches the formation of hydrates or solvates of inorganic salts at salt-melting temperatures, typically in the range of several hundred to greater than one thousand degrees Celsius. In contrast to West, the present invention is directed to hydrates of organic pyrimidine, pyridine or triazine derivatives formed at low temperatures. Hence, West is in a field that is quite different from that of the present invention.

Furthermore, the principles surrounding the formation of solvates or hydrates of inorganic salts are very different from that the principles surrounding the formation of solvates or hydrates of organic compounds, such as pyrimidines, pyridine or triazine derivatives. Inorganic salts in West form hydrates through ionic interaction at high salt-melting temperatures, whereas the hydrates of the organic compounds of the present invention are formed through van der Waals or hydrogen bonding interactions. Moreover, the high salt-melting conditions taught by West would result in the decomposition of organic compounds if such conditions were to be used in the formation of the organic hydrates of the present invention. Therefore, West is not reasonably pertinent to the particular problem with which Applicants were concerned. As such, West is not an analogous reference.

As stated above, the test for enablement is not whether any experimentation is necessary. The court states that the test is not merely quantitative, since a considerable amount of experimentation is permissive, if it is merely ***routine***, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (*see*, MPEP §2164.06).

Here, recrystallization is a routine method and well-known to a person of skill in the art for the isolation and purification of organic compounds. It is also a common observation, which is well-known to persons skilled in the art, that organic compounds form solvates or hydrates during the recrystallization and purification processes. For example, hydrates or solvates of the claimed compounds can be conveniently formed by recrystallization (*see*, page 15, paragraph 64 of the specification). Therefore, if anything, the formation of hydrates or solvates only requires a minimal amount of routine experimentation, which is permissible and not undue.

In concluding the formation of hydrates is unpredictable, the Examiner refers to an article by Vippagunta *et al.* (*Advanced Drug Delivery Reviews*, 2001, 48, 3-26, hereinafter "Vippagunta"), stating that predicting the formation of hydrate may be difficult. However, the article also points out that a large number of pharmaceutically active compounds, approximately one-third, are ***predictably*** capable of forming hydrates (*see*, Vippagunta, page 15). ***In fact, the interaction of drugs with water often results in the formation of hydrates*** (*see*, Stahl, "The problems of drug interactions with excipients," in D.D. Braimar, *Towards Better Safety of Drugs and Pharmaceutical Products*, Elsevier/North-Holland Biomedical Press, 1980, page 271, a copy of which is attached as Exhibit A). If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art (MPEP §2164.03). The compounds of the present invention have extended planar aromatic or heteroaromatic rings. It is well known in the art that such compounds have a tendency to crystallize. In particular, it is well known to a person skilled in the art that the nitrogen atom(s) in the aromatic rings can readily form hydrogen bonds with water, which facilitates the formation of hydrates (*see*, U.S. Patent No. 4,839,112, columns 2 and 3). Hydrogen bonding also plays an important role in the formation of hydrates of organic compounds (Lowry *et. al.*, Mechanism and Theory in Organic Chemistry, 4th Ed; page 283). Hence, based on the structure of the compounds, one skilled in the art can readily predict whether the compounds of the present invention will form hydrates. Thus, if anything, only reasonable and routine experimentation is needed to find out whether the compounds can form hydrates (*see*, page 15, paragraph 64 of the specification).

Working examples/amount of guidance. The Examiner also alleges that there are no working examples of a solvate or a hydrate. As set forth in MPEP §2164.02, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without undue experimentation. Here, as discussed above, those of skill in the art know that the compounds of the present invention have a tendency to crystallize and, if anything, only routine experiment is needed to isolate the hydrates and

confirm their compositions. Hence, undue experimentation is not required even in the absence of working examples.

Breadth of claim and quantity of experiment. The Examiner alleges that the amount of experiment would be undue because the genus embraces a large number of compounds. Again, Applicants respectfully disagree that the experiment will be undue. Although there are a number of compounds embraced by the formulae in the claimed invention, all of the compounds have similar planar hetero-aromatic ring structures containing one, two or three nitrogen atoms, which can readily form hydrogen bonds with water. A person skilled in the art will also recognize that minor variations of the substituents is unlikely to have significant effects on the formation of hydrates. Therefore, if anything, a person of skill in the art only needs to conduct routine experimentation to determine whether the compounds form hydrates and to confirm their compositions.

In view of the fact that undue experimentation is not required for the formation of solvates or hydrates of the claimed compounds, the solvates or hydrates of the claimed compounds do, in fact, meet the enablement requirement. Accordingly, Applicants respectfully request that the enablement rejection of the solvates or hydrates under 35 U.S.C. §112 be withdrawn.

3. Claim 17

Claim 17 was rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabled for compounds, wherein R^2 is a halo, or for compounds, wherein R^3 is substituted with a reactive functional group as recited for the compounds of claim 1. In order to expedite prosecution, Applicants have amended claim 17. Thus, to the extent that the rejection is applicable to amended claim 17, Applicants respectfully traverse this rejection.

In view of the amendment to claim 17, the enablement rejection directed to the reaction of compound (2) with compound (3) or compound (4), wherein R^2 is halo is overcome. Moreover, contrary to the Examiner's allegation, Applicants submit that the reaction of compound (2) with compound (3) or compound (4) is also enabled for the embodiments wherein R^3 is a reactive functional group because Reference 2 and exemplary compounds 1-126 teach

that R^3 can be a number of reactive functional groups including, but not limited to, heteroaryl, halide, amide, ester, hydroxy, amino, sulfonylamido, cyano, nitro, carboxylic acid, aldehyde, ketone, sulfonyl, hydrazine, amine oxide and oxime (*see*, pages 21 and 29-44 of the specification).

Moreover, Applicants assert that the reaction of compound (2) with reagent (5) or (6) is clearly enabled for the embodiments wherein R^2 and Q are both halo groups as Reference 1 teaches the mono-substitution reaction of a 4,6-dihalopyrimidine with reagent (5) or (6) (*see*, page 21, paragraphs 92-93 of the specification). Furthermore, embodiments wherein Q contains reactive halo groups can also be found in compounds 36, 38 and 90 (*see*, pages 31 and 38 of the specification).

Moreover, Applicants assert that newly added claim 18 is enabled as Reference 3 teaches the selective substitution of one of the halo groups of compound (2), wherein R^2 and Q are both halo functional groups, can be accomplished using a zinc reagent (7) (*see*, pages 21-22, paragraphs 96-98 of the specification).

Contrary to the Examiner's assertion, claim 17 is also enabled for reactions wherein R^3 contains a variety of reactive functional groups. Numerous examples set forth in the specification have demonstrated that compounds wherein R^3 contains various reactive functional groups, such as heteroaryl, halide, amide, ester, hydroxy, amino, sulfonylamido, cyano, nitro, carboxylic acid, aldehyde, ketone, sulfonyl, hydrazine, amine oxide, urea or oxime, can be readily prepared in accordance with the methods of the present invention. Compounds 36, 38, 43, 90 and 110 show that R^3 can contain a reactive halo group. References 2 and 3 show that R^3 can contain a carboxylic acid or an ester functional group. Compounds 1, 2, 6, 8-9, 14, 38-39, 53, 55-78, 80-85, 90-94, 96-106, 109-112, 114-121 and 123 all demonstrate that R^3 can contain an amide functionality. Compounds 3, 11, 12, 14, 25-29, 31-37, 40, 43-51, 108, 112, 122 and 124-126 show that R^3 can contain a heteroaryl functionality. Compounds 4, 7, 9, 10, 12, 15-18, 20, 24, 30, 37, 44-51, 56-57, 65, 69, 76, 78-79, 84-85, 95, 100-101, 105, 109, 115, 117, 120-122, 124-126 show that R^3 can contain an amino group. Compounds 56, 74 and 121 show that R^3 can contain hydrazine functionality. Example 5 demonstrates that R^3 can contain a sulfonyl

functional group. Compounds 13, 54 and 87-88 show that R^3 can contain a sulfonamide functionality. Compounds 8, 14, 17, 20, 23, 46, 61, 68, 71, 82, 85, 92, 102, 105, 113-114, 118, 123 and 126 show that R^3 can contain one or more hydroxyl functional groups. Compound 25 demonstrates that R^3 can contain an amine oxide functionality. Compounds 39, 41 and 52 show that R^3 can contain a ketone functionality. Compound 86 shows that R^3 can contains an urea functionality. Compound 42 shows that R^3 can contain an oxime functionality. Compounds 107 and 108 show that R^3 can contain an aldehyde functionality. Compound 111 shows that R^3 can contain a cyano functional group. Thus, the specification provides numerous examples that support the fact that the claims areenabled for reactions wherein R^3 contains a wide variety of reactive functional groups.

In view of the foregoing amendment and remarks, Applicants respectfully submit that claim 17 and newly added claim 18 are fully enabled for the scope of the claims. Accordingly, Applicants urge the Examiner to withdraw this rejection.

4. Claims 12-16

Claims 12-16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for treating tumoral diseases as recited in the claims. The Examiner takes the position that claim 12 encompasses thousands of cancers and the claimed method of treating is solely based on the inhibitory activity disclosed for the compounds. Applicants respectfully traverse the rejection.

Claims 12-14. In order to expedite prosecution, claim 12 has been amended to recite a method of treating a subject suffering from leukemia, the method comprising administering to the subject in need of such treatment an effective amount of a compound of claim 1, wherein the compound of claim 1 inhibits Bcr-abl. Applicants respectfully submit that validation of Bcr-able as a therapeutic target for the treatment of leukemia has long been established with the clinical success of imatinib (STI571, Gleevec, Novartis Pharma) (*see*, Capdeville *et al.*, *Nature Reviews:Drug Discovery*, 1:493-502 (2002), a copy of which is attached for the convenience of the Examiner as Exhibit B). Imatinib is a phenylaminopyrimidine that inhibits the activity of Bcr-able by binding to the ATP site and an

adjacent allosteric site to effectively lock the kinase in an inactive confirmation, thereby preventing transfer of phosphate from ATP to target protein. Clearly, Bcr-able is

As set forth in the specification and the attached paper (Adrian *et al.*, Nature Chemical Biology, 2(2):95-102 (Exhibit C)), which is co-authored by the Applicants of the present application, the compounds of the present invention are a new class of Bcr-abl inhibitors that possess excellent selectivity toward Bcr-abl-transformed cells and maintain potency against clinically relevant imatinib-resistant Bcr-abl mutants. Importantly, it is believed that this class of Bcr-abl inhibitors exert their activity through a newly described allosteric mechanism that involves binding to the myristoyl pocket. In view of their ability to inhibit Bcr-abl, which again is a validated therapeutic target for the treatment of leukemia, the compounds of the present invention can be used to treat leukemia. Thus, Applicants respectfully submit that amended claim 12 is fully enabled by the specification as originally filed. Accordingly, Aplicants respectfully request that the enablement rejection of claim 12 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 15-16. In traversal of the rejection, Applicants submit that claims 15-16 are fully enabled by the specification as filed. As set forth in the Example Section of the present application (*see, e.g.*, pages 44-45) as well as the attached Adrian *et al.* reference, the compounds of the present invention are a new class of Bcr-abl inhibitors that have the ability to selectively inhibit the proliferation of Bcr-abl-transformed cells and have anti-proliferative activity on Ba/F3 cells expressing either wild type or mutant forms of Bcr-abl. The examples also demonstrate that the compounds of the present invention, which inhibit the proliferation of the Bcr-abl expressing cells, inhibit cellular Bcr-abl autophosphorylation in a dose-dependent manner. Therefore, claims 15-16 are fully enabled by the specification as originally filed. Accordingly, Aplicants respectfully request that the enablement rejection of claims 15-16 under 35 U.S.C. §112, first paragraph, be withdrawn.

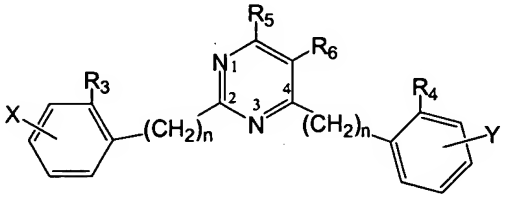
III. Rejections under 35 U.S.C. § 102(b)

A. Rejection of Claims 1, 6-8 and 11 Over Boykin et al.

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Boykin et al. (U.S. Pat. No. 5,686,456, hereinafter "Boykin"). Applicants respectfully traverse the rejection.

As set forth in MPEP §2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

Applicants assert that Boykin does not teach each and every element of the claimed invention. Boykin discloses pyrimidine derivatives having the structure:

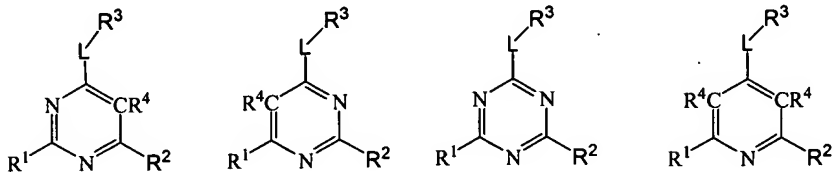


wherein n is a number from 0 to 2. The two substituents at the 2 and 4 positions of the above Boykin structure are either aryl (n = 0) or arylalkyl (n = 1 or 2) groups. Boykin does not teach substituents at the 2 and/or 4 position that are hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in claim 1. Hence, Boykin does not teach the compound of Formula I recited in claim 1 and, thus, claim 1 is not anticipated by Boykin. Since claims 6-8 and 11 are dependent from claim 1 and therefore incorporate all the limitations of claim1, claims 6-8 and 11 are not anticipated by Boykin. Accordingly, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 over Boykin under 35 U.S.C. §102(b) be withdrawn.

B. Rejection of claims 1, 6-8 and 11 over Carling et al.

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Carling *et al.* (U.S. Patent No. 5,763,448, hereinafter "Carling"). Applicants respectfully traverse the rejection.

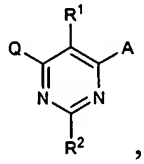
With X^1 and X^2 being nitrogen and/or a substituted carbon, the compound of Formula I can have four possible core structures, *i.e.*, $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ and $\mathbf{I^D}$, as illustrated below:



$\mathbf{I^A}$ $\mathbf{I^B}$ $\mathbf{I^C}$ $\mathbf{I^D}$

wherein R^2 is selected from the group consisting of hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy; and L is a bond, -O- and -NR^5-, wherein R^5 is hydrogen or C_{1-4}alkyl.

Applicants assert that none of the core structures $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ or $\mathbf{I^D}$ are anticipated by Carling because Carling does not teach each and every element of the claimed invention. Carling discloses a compound, *i.e.*, a pyrimidine derivative, having the formula:



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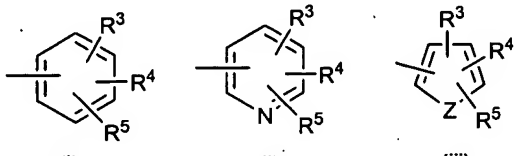
wherein Q represents a substituted five- or six-membered monocyclic hetero-aliphatic ring, which contains one nitrogen atom as the sole heteroatom and is linked to the pyrimidine ring via a carbon atom; and A represents a group of formula (i), (ii) or (iii):



(i) (ii) (iii) ,

wherein Z represents oxygen, sulfur or NH. Structures $\mathbf{I^C}$ and $\mathbf{I^D}$ are clearly not anticipated by Carling because $\mathbf{I^C}$ and $\mathbf{I^D}$ are triazine and pyridine derivatives, respectively, which are clearly not pyrimidine derivatives as disclosed by Carling.

Applicants assert that Carling does not teach structure $\mathbf{I^A}$. Substituents Q and A on the pyrimidine ring in Carling occupy the positions, which correspond to substituents L-R^3 and R^2 in structure $\mathbf{I^A}$. Carling does not disclose either Q or A being a bond, O or NR^5 as recited

for L in structure $\mathbf{I}^{A}$. Neither does Carling disclose Q or A being hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I}^{A}$. As such, structure $\mathbf{I}^{A}$ is not anticipated by Carling.

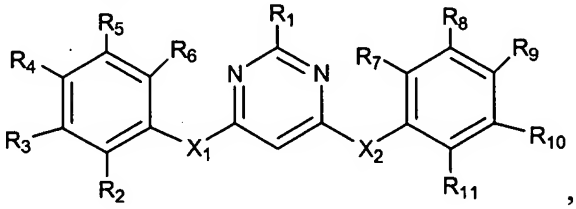
Applicants further assert that Carling does not teach structure $\mathbf{I}^{B}$. Substituents Q and A on the pyrimidine ring in Carling occupy the positions that correspond to substituents L-R^3 and R^1 in structure $\mathbf{I}^{B}$. Carling does not disclose (or allow for) the possibility of either Q or A being a bond, O or NR^5 as recited for L in core structure $\mathbf{I}^{B}$. Hence, Carling does not teach structure $\mathbf{I}^{B}$, and, thus, structure $\mathbf{I}^{B}$ is not anticipated by Carling.

Since core structures $\mathbf{I}^{A}$, $\mathbf{I}^{B}$, $\mathbf{I}^{C}$ or $\mathbf{I}^{D}$ of the compounds of Formula I are not disclosed by Carling, claim 1 is not anticipated by Carling. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Carling be withdrawn. Moreover, since claims 6-8 and 11 are dependent from claim 1 and, therefore, incorporate all the limitations of claim1, claims 6-8 and 11 are not anticipated by Carling. Accordingly, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 over Carling under 35 U.S.C. §102(b) be withdrawn.

C. Rejection of claims 1, 6, 9, 10 and 17 over Cuccia et al.

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cuccia *et al.* (U.S. Patent No. 6,281,219, hereinafter "Cuccia"). To the extent that the rejection is applicable to amended claim 1, Applicants respectfully traverse the rejection.

Applicants assert that Cuccia does not teach each and every element of the claimed invention and, thus, Cuccia does not anticipate the claimed invention. Cuccia teaches pyrimidine derivatives having the formula:



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wherein R_{10} is halogen, halo(C_{1-6})alkyl, halo(C_{2-6})alkenyl or halo(C_{2-6})alkynyl; and X_1 and X_2 are independently selected from the group consisting of NR_{14}, NR_{15}, O, CH_2, $CR_{18}R_{19}$, CO and $C{=}NOR_{20}$. As discussed above, the compound of Formula I of claim 1 has four possible core structures, *i.e.*, $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ and $\mathbf{I^D}$. Structures $\mathbf{I^C}$ and $\mathbf{I^D}$ are clearly not anticipated by Cuccia because $\mathbf{I^C}$ and $\mathbf{I^D}$ are triazine and pyridine derivatives, respectively, which are not pyrimidine derivatives as disclosed by Cuccia.

Moreover, Applicants assert that Cuccia does not teach a compound of core structure $\mathbf{I^A}$. Substituents X_1-aryl and X_2-aryl on the pyrimidine ring in Cuccia occupy the positions that correspond to R^2 and L-R^3 in $\mathbf{I^A}$. Cuccia does not teach substituents X_1-aryl and X_2-aryl being hydrogen, halo, amino, C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^A}$. Therefore, a compound of the structure $\mathbf{I^A}$ is not anticipated by Cuccia.

Applicants further assert that Cuccia does not teach a compound of core structure $\mathbf{I^B}$. Substituents X_1-aryl and X_2-aryl on the pyrimidine ring in Cuccia occupy the positions that correspond to R^1 and L-R^3 in structure $\mathbf{I^B}$. Cuccia teaches R_{10} being a halo or halo(C_{1-6})alkyl in a *meta* position with respect to X_2. Amended claim 1 does not allow for such a substitution pattern. Therefore, a compound of the structure $\mathbf{I^B}$ is not anticipated by Cuccia.

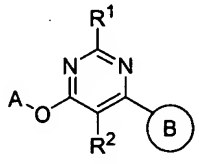
Since core structures $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ or $\mathbf{I^D}$ of the compounds of Formula I are not disclosed by Cuccia, claim 1 is not anticipated by Carling. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Cuccia be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim1, claims 6, 9, 10 and 17 are not anticipated by Cuccia. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Cuccia under 35 U.S.C. §102(b) be withdrawn.

D. Rejection of Claims 1, 6, 9, 10 and 17 over Wood *et al.*

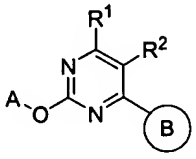
Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wood *et al.* (U.S. Patent No. 6,306,866, hereinafter "Wood"). To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

Applicants assert that Wood does not teach each and every element of the invention. Specifically, as explained below, Applicants submit that none of the compounds having the structures $\mathbf{I}^{A}$, $\mathbf{I}^{B}$, $\mathbf{I}^{C}$ or $\mathbf{I}^{D}$ are anticipated by Wood.

Wood teaches pyrimidine derivatives having the formulae:



IA



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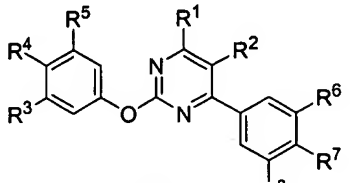

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wherein A represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsuphinyl, alkylsulphonyl and SF_5 groups. B represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsulphinyl, alkylsulphonyl and SF_5 groups.

1. Formula **IA**

Applicants submit that claim 1 is not anticipated by a compound of the formula **IA** as disclosed in Wood because none of the core structures $\mathbf{I}^{A}$, $\mathbf{I}^{B}$, $\mathbf{I}^{C}$ or $\mathbf{I}^{D}$ are disclosed in Wood.

Structure $\mathbf{I}^{A}$. Applicants assert that the core structure $\mathbf{I}^{A}$ is not anticipated by a compound of formula **IA** in Wood. Substituents A-O and B on the pyrimidine ring in **IA** occupy the positions that correspond to R^2 and L-R^3 in structure $\mathbf{I}^{A}$. Formula **IA** in Wood does not teach (or allow for) substituents A-O and B to be hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I}^{A}$. Instead, substituents A-O and B in formula **IA** in Wood are substituted-phenoxy or substituted-phenyl groups, respectively. Thus, neither substituent A-O nor B of the formula **IA** anticipates substituent R^2 in $\mathbf{I}^{A}$. As such, structure $\mathbf{I}^{A}$ is not anticipated by a compound of the formula **IA** in Wood.

Structure $\mathbf{I^B}$. Applicants also assert that structure $\mathbf{I^B}$ is not anticipated by a compound of formula **IA** in Wood. Substituents A-O and B on the pyrimidine ring in **IA** occupy the positions that correspond to R^1 and L-R^3 in core structure $\mathbf{I^B}$. Formula **IA** in Wood does not teach (or allow for) substituents A-O and B to be C_{3-8}heterocycloalkyl-C_{0-4}alkyl, heteraryl, heteroarylalkyl, or arylalkyl as recited for R^3 in structure $\mathbf{I^B}$. Substituents A-O and B in formula **IA** are substituted phenoxy and substituted phenyl groups, respectively. Therefore, neither substituent A-O nor B of the formula **IA** anticipates substituent R^3 in $\mathbf{I^B}$. As such, compounds of the structure $\mathbf{I^B}$ are not anticipated by a compound of formula **IA** in Wood.

Structure $\mathbf{I^C}$ and $\mathbf{I^D}$. Applicants assert that compounds of the structure $\mathbf{I^C}$ or $\mathbf{I^D}$ are not anticipated by compounds of formula **IA** in Wood. Compounds of the structure $\mathbf{I^C}$ or $\mathbf{I^D}$ are triazine or pyridine derivatives, respectively. Formula **IA** describes pyrimidine derivatives. Therefore, compounds of structure $\mathbf{I^C}$ or $\mathbf{I^D}$ are not anticipated by compounds of formula **IA** in Wood.

2. Formula **IB**.

Applicants submit that claim 1 is not anticipated by compounds of formula **IB** in Wood because none of the compounds having structures $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ or $\mathbf{I^D}$ are anticipated by the compounds of formula **IB**.

Structure $\mathbf{I^A}$. Applicants assert that compounds of structure $\mathbf{I^A}$ are not anticipated by the compounds of formula **IB** in Wood. Substituents R^1 and B on the pyrimidine ring in formula **IB** in Wood occupy the positions that correspond to L-R^3 and R^2 in structure $\mathbf{I^A}$. Formula **IB** teaches that at least one of R^1 and B is a substituted phenyl group. Formula **IB** does not teach (or allow for) a substitution pattern, wherein neither R^1 nor B is a substituted phenyl group as recited in structure $\mathbf{I^A}$. Hence, the compounds of structure $\mathbf{I^A}$ are not anticipated by compounds of formula **IB** in Wood.

Structure $\mathbf{I^B}$. Applicants assert that compounds of structure $\mathbf{I^B}$ are not anticipated by compounds of the formula **IB** in Wood. Substituent A-O in formula **IB** of Wood corresponds to substituent R^2 in structure $\mathbf{I^B}$. Substituent A-O in formula **IB** teaches a substituted phenoxy group, but does not teach hydrogen, halo, amino, C_{1-4}alkyl, halosubstituted C_{1-4}alkyl, C_{1-4}alkoxy

or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^B}$. Therefore, compounds of the structure $\mathbf{I^B}$ are not anticipated by the compounds of formula **IB** in Wood.

Structure $\mathbf{I^c}$ and $\mathbf{I^D}$. Applicants assert that a compound of structure $\mathbf{I^C}$ or $\mathbf{I^D}$ is not anticipated by a compound of formula **IB** in Wood. The compounds of structures $\mathbf{I^C}$ or $\mathbf{I^D}$ are a triazine and a pyridine derivative, respectively. In contrast , the compound of the formula **IB** is a pyrimidine derivative. Therefore, a compound of structure $\mathbf{I^C}$ or $\mathbf{I^D}$ is not anticipated by a compound of formula **IB** in Wood

3. Formula **IB1**.

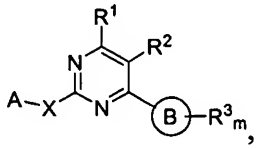
Using a similar analysis to that set forth above for a compound of formula **IB**, Applicants respectfully point out that a compound of structure $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ or $\mathbf{I^D}$ is not anticipated by a compound of formula **IB1** in Wood.

Again, since claim 1 is not anticipated by any compound of formulae **IA**, **IB** or **IB1** disclosed in Wood, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Wood be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim1, claims 6, 9, 10 and 17 are not anticipated by Wood. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Cuccia under 35 U.S.C. §102(b) be withdrawn.

E. Rejection of claims 6, 9, 10 and 17 over Scheiblich et al.

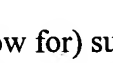
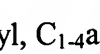
Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Scheiblich *et al.* (U.S. Patent No. 6,313,072 hereinafter "Scheiblich"). To the extent that the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

Applicants assert that Scheiblich does not teach each and every element of the claimed invention. Scheiblich teaches a compound having the formula:



wherein A represents an optionally substituted aryl group or an optionally substituted 5- or 6-membered hetero-aromatic group or a difluorobenzodioxolyl group; B represents a pheny, pyridyl or thienyl group; R^1 represents a halogen atom or a cyano or an optionally substituted alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, alkylamino or dialkylamino group; and X represents an oxygen or sulfur atom.

1. Structure $\mathbf{I^A}$

Applicants assert that Scheiblich does not teach a compound having the structure $\mathbf{I^A}$. Substituents R^1 and  in Scheiblich correspond to R^2 and L-R^3 in structure $\mathbf{I^A}$. Scheiblich does not teach (or allow for) substituents R_1 and  to be hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^A}$. Therefore, a compound of structure $\mathbf{I^A}$ is not anticipated by Scheiblich.

2. Structure $\mathbf{I^B}$.

Applicants assert that Scheiblich does not teach a compound having the structure $\mathbf{I^B}$. Substituent A-X in Scheiblich corresponds to R^2 in structure $\mathbf{I^B}$. Scheiblich does not teach (or allow for) A-X to be hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^B}$. Therefore, structure $\mathbf{I^B}$ is not anticipated by Scheiblich.

3. Structures $\mathbf{I^C}$ and $\mathbf{I^D}$.

Structures $\mathbf{I^C}$ and $\mathbf{I^D}$ recite a triazine and a pyridine derivative, respectively. Scheiblich discloses pyrimidine derivatives. Thus, compounds of structures $\mathbf{I^C}$ and $\mathbf{I^D}$ are not anticipated by Scheiblich.

Since core structures $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ or $\mathbf{I^D}$ of the compounds of Formula I are not disclosed by Scheiblich, claim 1 is not anticipated by Scheiblich. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Scheiblich be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim1, claims 6, 9, 10 and 17 are not anticipated by Scheiblich. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Scheiblich under 35 U.S.C. §102(b) be withdrawn.

III. Claim Rejections under 35 U.S.C. § 103(a)

A. Claim Rejection over Boykin

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Boykin. Applicants respectfully traverse the rejection.

> As set forth in MPEP §2142: To establish a prima facie case of obviousness, three criteria must be met. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations.

As explained above, Boykin does not teach all the claim limitations of claims 1, 6-8 and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Boykin compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Boykin be withdrawn.

B. Claim rejection over Carling

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Carling. Applicants respectfully traverse the rejection.

As explained above, Carling does not teach all the claim limitations of claims 1, 6-8 and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Carling compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Carling be withdrawn.

C. Claim rejection over Cuccia

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cuccia. Applicants respectfully traverse the rejection.

As explained above, Cuccia does not teach all the claim limitations of claims 1, 6, 9, 10 and 17. Moreover, in view of the structural differences between the presently claimed compounds and the Cuccia compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Cuccia be withdrawn.

D. Claim rejection over Wood

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wood. Applicants respectfully traverse the rejection.

As explained above, Wood does not teach all the claim limitations of claims 1, 6, 9, 10 and 17. Moreover, in view of the structural differences between the presently claimed compounds and the Wood compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Wood be withdrawn.

E. Claim rejection over Scheiblich

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Scheiblich. Applicants respectfully traverse the rejection.

As explained above, Scheiblich does not teach all the claim limitations of claims 1, 6-8, and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Scheiblich compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Scheiblich be withdrawn.

IV. Double Patenting

Claims 1 and 6-17 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 57-72 of co-pending Application No. 10/270,030.

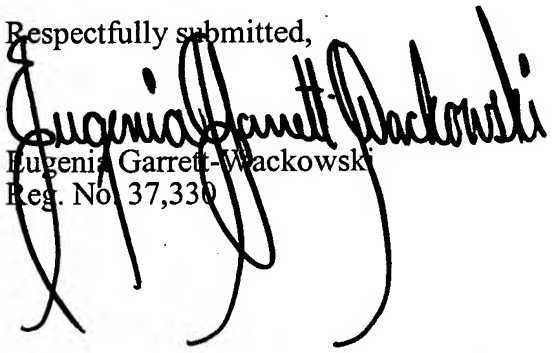
Because this is a provisional rejection, Applicants respectfully request that the Examiner hold this rejection in abeyance to this rejection until there is an indication of allowable subject matter. At that time, Applicants will cancel the conflicting claims or file a Terminal Disclaimer.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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